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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/240,675	02/02/99	BENOIT P	017283/0123

HM22/0903

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	7

DATE MAILED: 09/03/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/240,675	Benoit et al.
Examiner	**Group Art Unit**
S. Devi, Ph.D.	1641

☒ Responsive to communication(s) filed on *Jun 25, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *23-28* is/are pending in the application.

Of the above, claim(s) *27 and 28* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *23-26* is/are rejected.

☒ Claim(s) *23-26* is/are objected to.

☒ Claims *23-28* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) *08/307,588* .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *1*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 02/02/99 (paper no. 2 and 3) and 06/25/99 (paper no. 6). With these, Applicants have amended the specification.

Election

2) Acknowledgment is made of Applicants' election filed 06/25/99 (paper no. 5) of invention I, claims 23-26, in response to the restriction requirement mailed 05/26/99 (paper no. 4). Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P § 818.03(a)).

Claims Status

3) Claims 1-22 have been canceled via paper no. 3.

New claims 23-28 have been added via paper no. 3.

Claims 27 and 28 are withdrawn from further consideration by the Examiner of record, 37 C.F.R 1.142(b), as being drawn to a non-elected invention.

Elected claims 23-26 are under examination and an Action on the Merits for these claims is issued in the instant Office Action (paper no. 7).

Sequence Listing

4) Acknowledgment is made of Applicants' submission of Sequence Listing filed 06/25/99 (paper no. 6) which has been entered.

Information Disclosure Statement

5) Acknowledgment is made of Applicants' Information Disclosure Statement filed 02/02/99 (paper no. 1). The information referred to therein has been obtained from the parent case and considered. A signed copy is attached to this Office Action (paper no. 7).

Priority/Continuity Status

6) The instant application is stated to be a **Divisional** of application, SN 08/307,588, filed 12/05/94 in the amendment filed filed 02/02/99 (paper no. 2). However, an examination of the prior application, SN 08/307,588, indicates that the restriction requirement made by Examiner Martin was withdrawn by Examiner Loring in the Office Action 06/25/96 (paper no. 9 in case SN

08/307,588) since that application was filed under 35 U.S.C. 371. Moreover, claims drawn to peptides or polypeptides were not a part of the restriction requirement. Clarification is required. It is suggested that Applicants amend the first paragraph of instant specification to provide accurate information regarding the continuity/priority and the issued or pending status. For instance, application, SN 08/307,588, filed 12/05/94, has been issued as *US patent 5,919,453, and is a continuation of PCT/EP93/00770, which in turn claims foreign priority to the European application 92400902, filed 03/31/92.*

Drawings

7) The drawings are objected to under 37 C.F.R 1.84 because of the reasons set forth by the Draftsperson in the attached Form PTO 948. Correction is required.

Objection(s)

8) Claims 23-26 are objected to.

(a) In claim 23, "amino acid residue 27 to amino acid residue 427" represent a sequence of SEQ ID NO. 1 or 2. For clarity, it is suggested that Applicants replace the recitation with --the amino acid sequence 27-247--.

(b) Similar objections apply to claims 24 and 25.

(c) In claim 23, the parenthesis appears to be unnecessary.

(d) Claims 23 and 25 are objected to for the use of the abbreviation "IFN-R" in the claim language. It is suggested that Applicants use the full terminology at first occurrence with the abbreviation retained within the parentheses.

Claims Rejections - 35 U.S.C § 101

9) Claims 23-25 are rejected under as 35 U.S.C §101 as being directed to a non-statutory subject matter. The claims encompass a peptide or a polypeptide and therefore read on products of nature, i.e., naturally occurring peptide or polypeptide. The claims lack limitations which distinguish these products from those that may exist naturally. Consequently, the claims do not embody patentable subject matter as defined in 35 U.S.C § 101. See MEP. 2105. The rejection can be obviated by amending the claims to recite --An isolated peptide or polypeptide-- in connection with the products to reflect the hands of the inventors in the production or creation of

the recited products as is supported for at least one of the peptides, i.e. 27-427 of SEQ ID NO: 1 or 2, in the specification, for instance, in Example 1.

Claims Rejections - 35 U.S.C. § 112, First Paragraph

10) Claims 23-26 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure, because the specification does not provide evidence that the biological material encompassed in the scope of the claim is (1) known and readily available to the public; (2) reproducible from the written description, e.g. sequenced; or (3) deposited.

The instant claims are directed to a peptide or polypeptide which specifically binds to the monoclonal antibody, 64G12. It is apparent that the monoclonal antibody, 64G12, is required to practice the invention as claimed. As a required element, the recited hybridoma producing the monoclonal antibody must be known and be available to the public or obtainable by a reproducible method set forth in the specification without undue experimentation, or otherwise be readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the hybridoma producing the antibody recited in the claim. See 37 C.F.R 1.802. Without a publicly available deposit of this hybridoma, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed without undue experimentation.

Applicants indicate on page 10 of the instant specification that the monoclonal antibody, 64G12, has been deposited at the ECACC in February 199 and was assigned the accession number 92022605. However, no written assurance, either in the specification or in the form of a declaration is currently of record stating that all restrictions on the availability to the public of the hybridoma/antibody will be irrevocably removed upon grant of the Patent.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by Applicants or assignees, or a statement by an attorney of record who has authority and control over the conditions of the deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application is required. This requirement is necessary when deposits are made under the provisions of the Budapest

Treaty as the Treaty leaves this specific matter to the discretion of each state. As a possible means for completing the record, Applicants may submit a copy of the contract with the depository for the deposit and maintenance of the deposit.

Applicants' attention is directed to *In re Lundack*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 C.F.R § 1.801-1.809 for further information concerning deposit practice.

11) Claim 23 is rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a peptide or polypeptide consisting of the amino acid sequence 27-427 of SEQ ID NO. 1 or 2 (see Example 1), does not reasonably provide enablement for such a peptide or polypeptide which specifically binds to the monoclonal antibody 64G12 as claimed. As shown in Example 1, the instant disclosure is enabling for a peptide or polypeptide consisting of the amino acid sequence 27-427 of SEQ ID NO: 1 or 2. On page 10 of the instant specification, the monoclonal antibody, 64G12, is characterized as one which is "directed against an epitope on the amino-acid sequence comprised between amino-acid 27 and amino-acid 427 of the extracellular domain of the human IFN-R as represented on figure 2 SEQ ID Nos: 1-2". This descriptive support does not appear to be commensurate in scope with the evidence. For instance, the reactivity of the monoclonal antibodies is shown in Table 1. From the results of Table 1, it is not clear which amino acid sequence the monoclonal antibody, 64G12, is reacting with. The reactivity is stated to be "against the recombinant receptor" and "Cos" (see column 2). However, it is not clear which of the two enabled peptide or polypeptide sequences of SEQ ID NO: 1 or 2, (i.e. 7-427 and 1-427) the Cos cells are expressing. Absent evidence to the contrary, the entire scope of the instant claim is viewed as being non-enabled and therefore, the claim does not meet the enablement provision of 35 U.S.C. § 112, first paragraph. Undue experimentation would have been required by one of ordinary skill in the art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of clear guidance, the breadth of claims, and the quantity of experimentation necessary.

12) Claims 24 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a peptide or polypeptide consisting of the amino acid sequences 27-427 or 1-427 of SEQ ID NO: 1 or 2 (see Example 1), does not reasonably provide enablement for a peptide or polypeptide consisting of the amino acid sequence 27-229 or 1-229 of

SEQ ID NO: 1 or 2. The descriptive support on page 8 of the instant specification for a peptide comprising amino acid residue 1 to amino acid residue 229 of SEQ ID NO: 1 or 2 is not commensurate in scope with the evidence. Neither a descriptive, nor an evidentiary support appears to exist in the instant disclosure for a peptide or polypeptide consisting of the amino acid sequence 27-229 of SEQ ID NO: 1 or 2. Furthermore, no evidence is of record that peptides or polypeptides of these two claimed sequences, if produced, would bind specifically to the monoclonal antibody, 64G12. On page 10 of the instant specification, the monoclonal antibody, 64G12, is characterized as one which is "directed against an epitope on the amino-acid sequence comprised between amino-acid 27 and amino-acid 427 of the extracellular domain of the human IFN-R as represented on figure 2 SEQ ID Nos: 1-2". The reactivity of the monoclonal antibody 64G12 is shown in Table 1. From the results depicted in Table 1, it is not clear which amino acid sequence the monoclonal antibody, 64G12, is reacting with. The reactivity is stated to be "against the recombinant receptor" and "E. COLI" and "COS" (see column 2). However, it is not clear which of the two peptide or polypeptide sequences of SEQ ID NO: 1 or 2 enabled via Example 1 (i.e, 27-427 or 1-427), the Cos or *E. coli* cells are expressing. Note that the monoclonal antibody 64G12 does not react with *E. coli* cells. Absent evidence to the contrary, the entire scope of the instant claims is viewed as being non-enabled and therefore, the claims do not meet the enablement provision of 35 U.S.C. § 112, first paragraph. Undue experimentation would have been required by one of ordinary skill in the art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of guidance, the breadth of claims, and the quantity of experimentation necessary.

13) Claims 23-26 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims recite " a portion" of a peptide or polypeptide consisting of the amino acid sequences 27-427, 27-229 or 1-229 of SEQ ID NO: 1 or 2, or an analogue of the amino acid sequence 27-427, each binding specifically to the monoclonal antibody, 64G12. However, the instant specification is not enabled for such "a portion" of any of the amino acid sequences

recited, and for their binding specificity with the monoclonal antibody, 64G12. Without the disclosure of what is contained in this "portion", one of ordinary skill in the art cannot be sure of the sequences embraced by the claims. Without a showing that such a portion binds with the monoclonal antibody 64G12, one of ordinary skill in the art would not be able to practice the invention as claimed.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, a "portion" of the recited amino acid sequences comprising, for example, two amino acid residues are currently encompassed in the scope of the claims. However, there is no evidence that such a "portion" consisting, for example, of two amino acid residues would bind specifically to the monoclonal antibody, 64G12. Specific guidance for producing such a portion which retains its antibody-binding integrity is not provided. Further, binding of an undefined "portion" to a monoclonal antibody is not a predictable event. With a specification that is non-enabling, one of ordinary skill in the art would not be able to make and use the "portion" of the peptide or the polypeptide of the instant invention without undue experimentation.

Undue experimentation would have certainly been required by one of ordinary skill in the art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of specific guidance, the lack of working examples enabling a "portion" of the recited amino acid sequences capable of binding to 64G12 antibody, the unpredictability of such a portion to bind with a particular antibody, the breadth of claims, and the quantity of experimentation necessary.

14) Claim 26 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claim recites an " analogue" of a peptide or polypeptide consisting of the amino acid sequence 27-427 of SEQ ID NO: 1 or 2, which retains the ability to bind specifically to the monoclonal antibody, 64G12. However, the instant specification is not enabled for an "analogue" derived from the amino acid sequence 27-427 of SEQ ID NO: 1 or 2 by substitution of one or more amino acid residues, which further retains the ability to bind specifically to the monoclonal antibody, 64G12. The description on page 8 of the instant specification recites:

> According to another embodiment of the invention, the antibodies can be prepared against a polypeptide modified by substitution of one or more amino acids, provided that antibodies directed against the nonmodified extracellular domain of the IFN-R, recognize the modified polypeptide or peptide.

However, there is neither a descriptive, nor an evidentiary support for any "analogue" derived from the amino acid sequence 27-427 of SEQ ID NO: 1 or 2 having one or more defined substitution(s) that has the ability to bind specifically to the recited monoclonal antibody, 64G12. Without the disclosure of what this "analogue" encompasses and without specific guidance as to which amino acid residues in the recited amino acid sequence be retained in order to retain its antibody-binding ability and specificity, one of ordinary skill in the art cannot be sure of the sequences or amino acid residues embraced by the claim.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

With a specification that is non-enabling, one of ordinary skill in the art would not be able to make and use the "analogue" of the peptide or the polypeptide of the instant invention without undue experimentation.

Undue experimentation would have certainly been required by one of ordinary skill in the

art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of specific guidance, the lack of working examples enabling an "analogue" of the recited peptide or polypeptide, the breadth of claims, the unpredictability of such an analogue to bind with the specific antibody, and the quantity of experimentation necessary.

Claims Rejections - 35 U.S.C. § 112, Second Paragraph

15) Claims 23-26 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 23-26 are vague and indefinite in the recitation "a portion thereof" because it is not clear what is encompassed in this "portion", or how many amino acid residues are contained in this "portion". With the "portion" in question not being defined, the reader of the claim is not able to envisage the scope. It must also be noted that two amino acids, for example, represent a "portion" of the recited amino acid sequence. Would a peptide consisting of such a portion bind specifically to the monoclonal antibody 64G12? Clarification is required.

(b) Claim 26 is confusing and indefinite in the recitation "analogue" derived from a peptide or polypeptide by substitution of one or more amino acid residues which retains the ability to bind specifically to the monoclonal antibody 64G12. With the "analogue" in question not being defined, the reader of the claim is not able to envisage the scope. It is not clear whether substitution of any one or more amino acid residues anywhere in the amino acid sequence 27-427 would retain the functional ability of the analogue to bind to the monoclonal antibody 64G12.

Relevant Prior Art

16) The prior art made of record and not relied upon currently in any of the rejections are considered pertinent to Applicants' disclosure.

- Eid *et al.* (FR 2 657 881 A1)
- Benoit *et al.* (EP 0 563 487 A1)
- Uze *et al.* (*Cell* 60: 225-234, January 1990) teach the amino acid sequence of the human IFN-α receptor cDNA (see Figure 5). Specific peptide sequences, for example, a

sequence comprising amino acids 456-476 (see page 229, right column) or a cytoplasmic sequence comprising 100 amino acid residues (see page 231), and overlapping cDNAs isolated from the human Daudi cDNA library (see page 233) are taught.

- Eid *et al.* (WO 9218626) disclose a 436 or 427 amino acid fragments of the IFN receptors.
- Mogensen *et al.* (WO 91/05862 - Applicants' IDS) disclose a fragment of the human alpha receptor interferon and antibodies raised against the protein (see abstract).
- Colominici *et al.* (*PNAS* 87: 7230-7234, 1990 - Applicants' IDS) teach monoclonal antibodies reactive with the alpha subunit component of the IFNα receptor (see page 7233).

Remarks

17) Claims 23-27 stand rejected.

18) Papers related to this application may be submitted to Group 1600, AU 1641 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1 (CM1). The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242.

19) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 8.00 a.m to 4.00 p.m.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

August 1999

James C. Housel
JAMES C. HOUSEL 8/30/99
SUPERVISORY PATENT EXAMINER